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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/756,590	01/08/2001	Stewart Russell Jurgensen	P-4993	5633

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EXAMINER

TRAN, MY CHAU T

ART UNIT	PAPER NUMBER
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1639

DATE MAILED: 06/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/756,590	Applicant(s) JURGENSEN ET AL.	
	Examiner MY-CHAU T. TRAN	Art Unit 1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 February 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 39-60 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 39-60 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 22 May 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Handwritten signature/initials

DETAILED ACTION

Application and Claims Status

1. Applicant's amendment and response filed 02/16/2005 is acknowledged and entered. Claims 39, 40, and 60 have been amended.
2. Claims 39, 40, 44-50, and 54-60 were amended by the amendment filed on 09/02/2004, and 09/03/2004.
3. Claims 1-38 were canceled and Claims 39-60 were added by the amendment filed on 07/21/2004.
4. Claims 4, 6, 10-12, and 23 were canceled; Claims 1, 7, 13, 15, 18, 19, and 31 were amended; and Claims 37 and 38 were added by the amendment filed on 07/18/2003.
5. Claims 23 and 32 were canceled and Claims 1, 5-7, 19, 21, and 31 were amended by the amendment filed on 12/30/2002.

Maintained Rejection(s)

6. Claims 39-60 are pending.

Claim Rejections - 35 USC § 112

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7. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

8. Claims 39-60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase “substantially absent” in claim 39 is considered indefinite because it is unclear as to the means of measuring the degree of “substantially”. It is unclear what constitutes the metes and bounds of “substantially absent”, i.e. what degree is considered “substantially absent”? 25%? 50%? 100%?

Claim Rejections - 35 USC § 103

9. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

10. Claims 39-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Levine et al. (US Patent 5,776,710; which is referred to as Levine ‘710) and Levine et al. (US Patent 5,393,674; which is referred to as Levine ‘674).

Claim 39 recites a method. The method comprises the step of: 1) placing the biological sample into a separation container; 2) centrifuging the separation container containing the biological sample to densitometrically separate components of the biological sample into layers, wherein the elongated target layer is located within the focusing device of the separation container; and 3) aspirating the elongated target layer to remove the desired component from the separation container.

The separation container comprises a) a focusing device, b) a first set of selection microbeads, and c) a second set of selection microbeads. The first set of selection microbeads comprises a binding agent that specifically binds to the target, i.e. desired component, in the biological sample. The second set of selection microbeads comprises binding agent different from the binding agent of the first set of selection microbeads, and specifically binds to components other than the target, i.e. undesired components, in the biological sample. The

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focusing device has a specific density and upon centrifugation the focusing device move in a vertical direction and elongate the target layer.

The target layer comprises the first set of selection microbeads with the target, i.e. desired components, of the biological sample, and the target layer is elongated within the focusing device. The second set of selection microbeads with the undesired components is not located with the focusing device.

Levine '710 discloses the method for detecting a target analyte in a biological sample in a tube (see e.g. Abstract; col. 2, lines 35-64; claims 1-2). The method comprises the step of a) adding a group of capture bodies to the sample, which capture bodies have a specific gravity which ensures that said capture bodies will settle into a predetermined location in the sample in the tube, each capture body in said group being coupled with a binding material to form capture body couples which are specific to the target analyte; b) adding to said sample labeled antibodies or other binding material which are specific to said target analyte so as to form a capture body/labeled binding material sample mixture; c) intimately admixing said sample and said labeled binding material so as to form a capture body/labeled binding material sample mixture; d) incubating the capture body/labeled binding material sample mixture; and e) centrifuging/densimetrically the sample so as to aggregate the capture bodies into a distinct location in the tube (see e.g. Abstract; col. 3, lines 56-58; col. 7, lines 34-57; claims 1-2). The tube comprises one or more bodies or group of bodies such as inserts or plastic beads of different densities (see e.g. Abstract; col. 2, lines 43-49; col. 3, lines 10-15, and 33-37). Additionally, the features of remaining independent and dependent claims are either specifically described by the reference (e.g. type of biological sample), or constitute obvious variations in parameters which are routinely modified in the art (e.g. the density of the microbeads), and which have not been described as critical to the practice of the invention.

The method of Levine '710 differs from the presently claimed invention by failing to include the step of removing the desired component and a ribbed such that one or more axial passages exist in the focusing device.

Levine '674 disclose a method for harvesting target cells from centrifuged sample of blood contained in a tube which also contains a cylindrical float having a through passage for receiving and elongating layers of blood cell components to be harvested from the sample, the float having an axial constant outer diameter which ensures that the float fits snugly in the tube (see e.g. claim 1; fig. 1 and 4). The method steps of centrifuging the blood, tube, and float at sufficient G forces to move the float toward one end of the tube and forcing the blood cell components to settle in said through passage (see e.g. claim 1; fig. 1 and 4). The cells and components of the buffy coat layer are expanded linearly in the narrow bore channel in the float and thus can be easily harvested (see e.g. col. 3, lines 13-15). The method includes harvesting the target cells from the float bore (ref. #7 of fig. 5) with a needle (see e.g. col. 4, lines 55-57; fig. 5). Additionally, it is noted that figures 1 and 4 of Levine '674 are identical to figures 1 and 2 of the instant specification.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include the step of removing the desired component and a ribbed such that one or more axial passages exist in the focusing device as taught by Levine '674 in the method of Levine '710. One of ordinary skill in the art would have been motivated to include the step of removing the desired component and a ribbed such that one or more axial passages exist in the focusing device in the method of Levine '710 for the advantage of providing a ten fold expansion of the white cell and platelet layers when performing the cell harvesting with the

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tube-float combination (Levine '674: col. 2, lines 50-60) since both Levine '710 and Levine '674 disclose the method of cell separation by density gradient centrifugation (Levine '710: col. 2, lines 35-64; Levine '674: col. 1, lines 7-14; fig. 1 and fig. 4). Furthermore, one of ordinary skill in the art would have reasonably expectation of success in the combination of Levine '710 and Levine '674 because Levine '674 claimed the method for harvesting target cells from centrifuged sample contained in a tube which also contains a cylindrical float having a through passage for receiving and elongating layers of components to be harvested from the sample (Levine '674: claim 1 and 2).

New Rejection(s) - Necessitated by Amendment

Claim Rejections - 35 USC § 112

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 39-60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Withdrawn Rejection(s)

13. The rejections under 35 USC 112, second paragraph, of (a) thru (k) as being indefinite have been withdrawn in light of applicant's amendments of claim 39.

Claim 39 recite the phrase "substantially equal" to further the claimed focusing device by claiming that its property, density, is the similar to the property, density, of the claimed first set

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of selection microbeads. The term "substantially" is a relative term, which renders the claim indefinite and/or unclear. The term "substantially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. See also MPEP § 2173.05(b). Thus, claim 37 is indefinite and/or unclear.

Response to Arguments

14. Applicant's argument directed to the rejection under 35 U.S.C. 112, second paragraph, for claims 39-60 has been fully considered but they are not persuasive for the following reasons.

Applicant argues that the phrase "substantially absent" is not indefinite because "*the specification makes clear that the methods of the invention are designed to significantly enrich samples for target components "compared to many prior processes and have a substantially lower contaminant level of [contaminants]"*". Thus, the specification provides guidance for the phrase "substantially absent", and the phrase "substantially absent" is not indefinite.

Applicant's arguments are not convincing since the phrase "substantially absent" is indefinite because the specification does not provide any guidance for the phrase "substantially absent". The complete passage of the specification recited by applicant is that "*The tube, float and sample are centrifuged at a sufficient speed and for a length of time necessary to separate the constituents of the sample into layers and force the microbeads and the trapped target component into the axial bore of the float. The sample can be centrifuged at a speed to provide sufficient centrifugation force to cause separation of the layers. The tube is slowly stopped and removed from the centrifuge. A needle or cannula then pierces the stopper and is inserted into*

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the axial bore to remove the sample containing the microbeads. The harvested sample is further processed and analyzed by various processes as known in the art. In one embodiment, the harvested cells are analyzed using a flow cytometer. The rare cells or other target components can be washed and separated from the microbeads and the binding antibody by known methods. The resulting harvested rare cells are significantly enriched compared to many prior processes and have a compared to many prior processes and have a substantially lower contaminant level of red and white blood cells” (pg. 14, line 18 thru pg. 15, line 4). This passage does not provide any guidance with regard to the phrase “substantially absent” for the claimed limitation that the “components other than at least one target component of the biological sample are substantially absent from the axial bore passage of the focusing device after centrifugation” (claimed step (b), line 6-9). Additionally, MPEP § 2173.05(b) states:

*Even if the specification uses the same term of degree as in the claim, a rejection may be proper if the scope of the term is not understood when read in light of the specification. While, as a general proposition, broadening modifiers are standard tools in claim drafting in order to avoid reliance on the doctrine of equivalents in infringement actions, when the scope of the claim is unclear a rejection under 35 U.S.C. 112, second paragraph, is proper. See *In re Wiggins*, 488 F. 2d 538, 541, 179 USPQ 421, 423 (CCPA 1973).*

When relative terms are used in claims wherein the improvement over the prior art rests entirely upon size or weight of an element in a combination of elements, the adequacy of the disclosure of a standard is of greater criticality.

That is the scope of the phrase “substantially absent” is not understood when read in light of the specification. Thus, the phrase “substantially absent” is indefinite, and the rejection is maintained.

15. Applicant's arguments directed to the rejection under 35 USC 103(a) as being unpatentable over Levine et al. (US Patent 5,776,710; which is refers to as Levine ‘710) and

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Levine et al. (US Patent 5,393,674; which is refers to as Levine '674) for claims 39-60 were considered but they are not persuasive for the following reasons.

Applicant contends that the combine teaching of Levine et al. (which is refers to as Levine '710) and Levine et al. (which is refers to as Levine '674) is not obvious over the presently claimed method because 1) *“the methods of Levine '710 result in the analyte being trapped, or sandwiched, and affixed to the surface of a tube insert”*, i.e. the analyte is immobile; 2) *“Levine '674 does not teach, mention or even suggest that microbeads or particulate carriers be used in conjunction with the float.”*; 3) there is no motivation and /or expectation of success for the combination of the references. Therefore, the combine teaching of Levine et al. (which is refers to as Levine '710) and Levine et al. (which is refers to as Levine '674) is not obvious over the presently claimed method.

Applicant's arguments are not convincing since the combine teaching of Levine et al. (which is refers to as Levine '710) and Levine et al. (which is refers to as Levine '674) is obvious over the presently claimed method.

First, in response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Additionally, the presently claimed method would result is trapping and immobilizing the analyte, i.e. *“wherein a target layer comprising the first set of selection microbeads bound to at least one target component is located within the axial bore passage of the focusing device”* see claimed step (b), lines 2-5.

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Second, in response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the motivation to combine the teaching of Levine et al. (which is refers to as Levine '710) and Levine et al. (which is refers to as Levine '674) is found in the teaching of Levine '674, i.e. the advantage of providing a ten fold expansion of the white cell and platelet layers when performing the cell harvesting with the tube-float combination (Levine '674: col. 2, lines 50-60).

Third, in response to applicant's argument that there is no reasonable expectation of success to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is a reasonable expectation of success, i.e. obviousness does not require absolute predictability, however, at least some degree of predictability is required. (See MPEP 2143.02). In this case, there is some degree of predictability in the combine the teaching of Levine et al. (which is refers to as Levine '710) and Levine et al. (which is refers to as Levine '674) since both disclose 'trapping' the analyte within the cylindrical plastic float or insert (Levine '710: col. 2, lines 35-64; Levine '674: col. 1, lines 7-14; fig. 1 and fig. 4). Thus, there is some degree of predictability in the combine the teaching of Levine et al. (which is refers to as Levine '710) and Levine et al. (which is refers to as Levine '674).

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Thus, the combine teaching of Levine et al. (which is refers to as Levine '710) and Levine et al. (which is refers to as Levine '674) is obvious over the presently claimed method, and the rejection is maintained.

Conclusion

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to My-Chau T. Tran whose telephone number is 571-272-0810. The examiner can normally be reached on Monday: 8:00-2:30; Tuesday-Thursday: 7:30-5:00; Friday: 8:00-3:30.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

mct
May 29, 2005


PADMASHRI PONNALURI
PRIMARY EXAMINER